

**WHAT IS CLAIMED IS:**

1. A method of identifying a compound that increases expression of an endothelin converting enzyme (ECE) nucleic acid, the method comprising:  
 contacting cells comprising an ECE nucleic acid with a compound; and  
 detecting the amount of ECE RNA or ECE polypeptide in or secreted from said cell,  
 wherein an increase in the amount of ECE RNA or ECE polypeptide in the presence of said compound compared to the amount of ECE RNA or ECE polypeptide produced in the absence of said compound is an indication that said compound increases expression of said ECE nucleic acid.
2. The method of claim 1, wherein said cell is selected from the group consisting of H4 neuroglioma cells, CHO cells and HUVEC cells.
3. The method of claim 1, wherein said ECE nucleic acid comprises ECE promoter and/or regulatory sequences.
4. The method of claim 1, wherein said ECE nucleic acid comprises ECE coding sequences.
5. The method of claim 1, wherein the amount of said ECE RNA is determined by Northern blotting.
6. The method of claim 1, wherein the amount of said ECE polypeptide is determined by Western blotting.
7. A method of identifying a compound that increases the activity of an ECE polypeptide, the method comprising:  
 contacting A $\beta$  with an ECE polypeptide; and  
 detecting the amount of unhydrolyzed A $\beta$ ,

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wherein a decrease in the amount of unhydrolyzed A $\beta$  produced in the presence of said compound compared to the amount of unhydrolyzed A $\beta$  produced in the absence of said compound is an indication that said compound increases the activity of an ECE polypeptide.

8. The method of claim 7, wherein said ECE and said A $\beta$  are in a cell.

9. The method of claim 7, wherein said unhydrolyzed A $\beta$  is detected using an immunoassay.

10. A method of identifying a compound that increases catabolism of A $\beta$ , the method comprising:

performing a big ET conversion assay in the presence or absence of said compound,

wherein an increase in the amount of ET in the presence of said compound compared to the amount of ET in the absence of said compound is indicative of a compound that increases catabolism of A $\beta$ .

11. A method of identifying a compound that has anti-hypertension activity but does not cause an increase in the level of A $\beta$ , the method comprising:

contacting A $\beta$  with an ECE in the presence of said compound;

detecting the amount of unhydrolyzed A $\beta$ , wherein lack of an increase in the amount of unhydrolyzed A $\beta$  produced in the presence of said compound compared to the amount of unhydrolyzed A $\beta$  produced in the absence of said compound is an indication that said compound does not cause an increase in the level of said ECE; and

determining the anti-hypertension activity of said compound.

12. The method of claim 11, wherein the anti-hypertension activity of said compound is determined in an animal.

13. The method of claim 12, wherein said animal is a spontaneously hypersensitive rat (SHR).

14. A method of determining that an anti-hypertension compound or candidate compound does not cause an increase in the level of A $\beta$ , the method comprising:

contacting A $\beta$  with an ECE in the presence of said anti-hypertension compound or candidate compound; and

detecting the amount of unhydrolyzed A $\beta$ ,

wherein the lack of an increase in the amount of unhydrolyzed A $\beta$  produced in the presence of said compound compared to the amount of unhydrolyzed A $\beta$  produced in the absence of said compound is an indication that said compound does not cause an increase in the level of said ECE.

15. The method of claim 14, wherein said anti-hypertension compound or candidate compound is an ECE inhibitor.

16. A method of increasing intracellular or extracellular A $\beta$  catabolism, the method comprising: administering a compound to a cell, said compound decreasing or abolishing the activity of an inhibitor of an ECE polypeptide.

17. The method of claim 16, wherein said cell is *in vitro* or *in vivo*.

18. A method of increasing intracellular or extracellular A $\beta$  catabolism, the method comprising: administering a compound to a cell, said compound decreasing the intracellular or extracellular degradation of an ECE polypeptide.

19. The method of claim 18, wherein said cell is *in vitro* or *in vivo*.

20. A method of decreasing the amount of A $\beta$  in or secreted from a cell, the method comprising: administering a vector to said cell, said vector comprising an ECE nucleic acid and elements necessary for expression operably linked to said ECE nucleic

acid, wherein the ECE polypeptide encoded by said ECE nucleic acid hydrolyzes A $\beta$ , thereby decreasing the amount of A $\beta$  in or secreted from said cell.

21. The method of claim 20, wherein said cell is *in vitro* or *in vivo*.
22. A method of treating an individual having AD, the method comprising: administering a vector to said individual, said vector comprising an ECE nucleic acid and elements necessary for expression operably linked to said ECE nucleic acid.
23. The method of claim 22, wherein said vector is targeted to the brain of said individual.
24. A method of treating an individual having AD, the method comprising: administering an ECE polypeptide to said individual.
25. The method of claim 24, wherein said administration is to the brain of said individual.
26. An ECE-selective inhibitor, wherein cells are impermeable to said ECE-selective inhibitor.
27. An ECE-selective inhibitor, wherein the blood-brain barrier is impermeable to said ECE-selective inhibitor.
28. An isolated mutant ECE polypeptide.
29. The mutant ECE polypeptide of claim 28, wherein said mutant ECE polypeptide exhibits altered A $\beta$  hydrolysis properties compared to a corresponding wild-type ECE polypeptide.

30. The polypeptide of claim 29, wherein said altered A $\beta$  hydrolysis properties result in decreased catabolism of A $\beta$ .

31. The polypeptide of claim 29, wherein said altered A $\beta$  hydrolysis properties result in an accumulation of A $\beta$ .

32. The polypeptide of claim 29, wherein said altered A $\beta$  hydrolysis properties are associated with an increased risk for AD in an individual.

33. The polypeptide of claim 29, wherein said altered A $\beta$  hydrolysis properties results in or contributes to AD.

34. An isolated mutant ECE nucleic acid molecule.

35. The isolated mutant ECE nucleic acid of claim 34, wherein said ECE nucleic acid carries said mutation in a promoter and/or regulatory region.

36. The isolated mutant ECE nucleic acid of claim 34, wherein said ECE nucleic acid carries said mutation in the coding sequence.

37. A method of diagnosing an individual having AD or having an altered predisposition for AD, the method comprising:

detecting the presence or absence of a mutant ECE nucleic acid in a biological sample from said individual,

wherein the presence of said mutant ECE nucleic acid is indicative of an individual having AD or having an altered predisposition for AD.

38. The method of claim 37, wherein said altered predisposition for AD is an increased predisposition.

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